IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

IN RE: BRIMONIDINE PATENT LITIGATION	)	C.A. No. 07-MD-01866-GMS

APOTEX'S ANSWERING CLAIM CONSTRUCTION BRIEF

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INTRODUCTION

Pursuant to the Scheduling Order dated June 3, 2008, Defendants Apotex, Inc. and Apotex, Corp. (collectively, "Apotex") respectfully submit this Answering Claim Construction Brief with respect to its proposed claim constructions of U.S. Patent Nos. 5,424,078 ("the '078 patent"), 6,562,873 ("the '873 patent"), 6,627,210 ("the '210 patent"), 6,673,337 ("the '337 patent"), and 6,641,834 ("the '834 patent").

Apotex and Allergan, Inc. ("Allergan") agree on the claim construction of all claims of the '078, '873, '210, '337, and '834 patents asserted against Apotex. Exela PharmSci, Inc., Exela Pharm Sci Pvt., Ltd., Paddock Laboratories, Inc., and PharmaForce Inc. (collectively, "the Exela Defendants") have proffered their own constructions of claims 1 and 10 of the '834 patent, the only patent currently asserted against them. In the Exela Defendants' opening brief, they concede the only claim construction genuinely at issue is the construction of "about" in the limitation "a pH of **about** 7.0 or greater", which appears in both claims 1 and 10. Consistent with prior Federal Circuit and district court rulings regarding the ordinary and customary meaning of the term, this Court previously ruled "about" in the '834 patent claims mean "approximately". *Allergan Inc. v. Alcon Inc.*, No. 04-968 (GMS) (D. Del. July 26, 2005). The Exela Defendants' justification for having the Court redefine "about"—only with respect to the sole limitation genuinely at issue—is not supported by the prosecution history on which they rely. Therefore, this Court should find in favor of Apotex, holding "about" to mean "approximately".

ARGUMENT

I. The Exela Defendants Concede the Only Issue Presently Before the Court is the Construction of "About" in the Claim Limitation "a pH of About 7.0 or Greater"

The parties offer the following construction of claim 1:[1]

Asserted Claim of '834 Patent	Apotex's Proposed Construction	Exela's Proposed Construction
Claim 1		
1. A therapeutically effective aqueous ophthalmic composition comprising: up to about 0.15% (w/v) of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline tartrate,	The claim requires a therapeutically effective aqueous ophthalmic composition. The claimed composition comprises up to approximately 0.15% brimonidine tartrate.	A water-based formulation containing between 0% and about 0.15% (w/v) of brimonidine tartrate for ophthalmic administration that is demonstrated to provide a therapeutic benefit to a patient to whom the formulation is administered.
the composition having a pH of about 7.0 or greater,	The claimed composition has a pH of approximately 7.0 or greater.	The therapeutically effective formulation referred to above has a pH of 7.0 or greater within measurement tolerances. In no event can the claim cover a formulation having a pH of 6.8 or below.
and the 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline tartrate being soluble in the composition at about 21° C.	Agreed-upon construction - The brimonidine tartrate is soluble in the composition at approximately 21° C.	

In its opening brief, Apotex argued, with the exception of the "a pH of about 7.0 or greater" limitation, there was no discernable difference between the positions proffered by the

[1] Claim 10 is identical to claim 1, with the sole exception of replacing "5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline tartrate" in claim 1 with "a component selected from the group consisting of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline, esters of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline and mixtures thereof" in claim 10. (*See* D.I. 48 at 2-3.) There is no dispute between the parties regarding the construction of this language. Therefore, Apotex's arguments are made with respect to the common claim elements exemplified in claim 1, and any argument made with respect to claim 1 is equally applicable to claim 10.

Exela Defendants and the plain and ordinary meaning of the claims.[2] In particular, Apotex was unable to discern any difference between the Exela Defendants' construction of "therapeutically effective", "aqueous … composition" and "up to about 0.15% (w/v)" and the plain and ordinary meaning of the claims terms themselves. (D.I. 47 at 3-4.) Allergan apparently agrees. (*See* D.I. 49 at 18, ("Exela's motivation in rewording the claim language – which is already plain on its face – is unclear.").) As evidenced below, the Exela Defendants also appear to agree there is no difference between most of the disputed claim language and the construction they offer.

The Exela Defendants argue the first element of claim 1, namely "[a] therapeutically effective aqueous ophthalmic composition comprising: up to about 0.15% (w/v) of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline tartrate", should be afforded its plain and ordinary meaning. (D.I. 48 at 3-4, ("the Exela Defendants contend that the first element of claims 1 and 10 … be construed according to its straightforward, ordinary meaning.").) This is the same position taken by Apotex and Allergan. Still, the Exela Defendants redraft the claims, citing in one instance Merriam-Webster's Medical Dictionary in support of their use of "water-based formulation" in replacement of the straightforward "aqueous ... composition" language of the claim. *Id.* at 10. Apotex does not understand to what end the Exela Defendants seek to redraft the clear terms of the first element of claim 1.

As the Federal Circuit has made clear, "[i]n some cases, the ordinary meaning of claim language as understood by a person of ordinary skill in the art may be readily apparent even to lay judges, and claim construction in such cases involves little more than the application of the widely accepted meaning of commonly understood words." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1314 (Fed. Cir. 2005). This is such a case. The Court should reject the Exela Defendants'

[2] Because the Court had previously construed the meaning of "about" in the '834 patent, Apotex relied on this construction in its opening brief. Because the Exela Defendants ask the Court in their opening brief to reconsider its prior holding, Apotex responds to this argument herein.

attempts to redraft the first element of claim 1, as all parties agree this element should be afforded its straightforward, ordinary meaning.

II. The Prosecution History Relied on By the Exela Defendants Does Not Support Their Disclaimer Theory

The Exela Defendants' admit this Court's construction of "about" to mean "approximately" controls – at least, with respect to every usage of the term except its use in the "a pH of about 7.0 or greater" limitation (the "pH limitation"). The Exela Defendants argue "about" in the pH limitation should be construed to mean "a pH of 7.0 or greater within measurement tolerances". However, the Exela Defendants offer the Court no guidance as to what would or would not be "within measurement tolerances". Were the Court to adopt the Exela Defendants' definition, another round of claim construction would be required to construe the term's construction. Such an incongruous end should not be taken by this Court.

In its final argument, the Exela Defendants ask the Court to find Allergan disclaimed a pH of 6.8 or below.[3] The Exela Defendants' argue it is this disclaimer that justifies this Court revisiting its own prior construction of the term "about". (D.I. 48 at 12, ("While Alcon referenced Allergan's prosecution history arguments in its briefing, Alcon did not seek a construction that specifically incorporated Allergan's disclaimer of pH values below 6.8.").) But the disclaimer the Exela Defendants' claim is far from clear, as is required by law. *See Brookhill-Wilk 1, LLC v. Intuitive Surgical, Inc.*, 334 F.3d 1294, 1301 (Fed. Cir. 2003) ("Absent a **clear disclaimer** of particular subject matter, the fact that the inventor anticipated that the invention may be used in a particular manner does not limit the scope to that narrow context.") (Emphasis added).

[3] It is not clear if the Exela Defendants ask for this construction in the alternative, or if they otherwise believe a pH of 6.8 is "within measurement tolerances", necessitating the Court's holding a pH of 6.8 and below is disclaimed by the patentee.

As the sole support for its disclaimer theory, the Exela Defendants rely on the patentee's March 24, 2003 response to an examiner's December 18, 2001 office action. In that response, the patentee argued:

> The present invention is the result of the surprising finding that increasing the pH of a brimonidine solution to a pH of greater than about 7.0 leads to a similar efficacy at a 25% lesser concentration (from 0.2% (w/v) to about 0.15% (w/v) or less) than is seen in a brimonidine solution **at a pH of about 6.6-6.8**.

(Emphasis added). However, this response does not support the Exela Defendants' argument because the evidence the patentee submitted in support of these "surprising findings" showed the 0.2% (w/v) comparison solution was not a solution with a pH of about 6.6 to 6.8, but instead one of a pH about 6.3 to 6.5.

In the paragraph *immediately preceding* the disclaimer alleged by the Exela Defendants, the patentee argued, "[t]o appreciate the surprising aspects of the present invention it is important to understand that previous brimonidine solutions for ophthalmic use have been formulated at **a pH of about 6.3 – 6.5** and a concentration of 0.2% (w/v)." (Emphasis added). In the sentence *immediately following* the alleged disclaimer, the patentee argued, "[t]his appears to be due to the fact that at a pH closer to the pKa of brimonidine (which has a pKa of about 7.4) **than pH 6.3-6.5**, a larger proportion of the molecules are electrostatically neutral, and thus less lipophobic than the polarized molecule." (Emphasis added). The patentee appears to be comparing the 0.15% (w/v) solution at pH about 7.0 to a 0.2% (w/v) solution at a pH of 6.3 to 6.5.

As required under the PTO rules, the patentee supported its attorney argument with evidence. The evidence clearly shows the patentee was comparing a 0.2% (w/v) solution at a pH of 6.3 to 6.5 to a 0.15% (w/v) solution at a pH of 7.2:[4]

[4] The arguments appearing in the March 24, 2003 response are also instructive as to the patentee's use of the term "about" when talking about pH. These statements support the Court's prior ruling that "about" means "approximately".

> For the examiner's convenience, Applicants hereby attach a copy of an article by Katz, et al., *J. Glaucoma* 11:119 (April 2002) which shows the comparison of the 0.2% brimonidine formulation having **a pH 6.3-6.5** (the "0.2% formulation") with 0.15% brimonidine solution at pH 7.2 (the 0.15% formulation).
>
> Although the Katz paper does not disclose the pH of either solution, Applicants hereby enclose a Declaration of Amy Batoosingh, Director of Ophthalmological Clinical Research at Allergan, Inc. Ms. Batoosingh, whose work is contained within and acknowledged on page 126 of Katz, indicates her Declaration that the formulation "brimonidine 0.2%" in the Katz paper, which used benzalkonium choride as preservative, comprised 0.2% brimonidine **at pH 6.3-6.5**, and that the formulation termed "brimonidine-Purite 0.15%" in Katz, (which used oxy-chloro as a preservative) comprised 0.15% brimonidine at pH 7.2.

(Emphasis added). As the patentee correctly noted, Ms. Batoosingh's declaration explains a 0.2% (w/v) brimonidine solution at pH 6.3 to 6.5 - and not pH 6.6 to 6.8 - was being compared to a 0.15% brimonidine solution at pH 7.1 to 7.3 in the Katz article. The Katz article (supplemented by Ms. Batoosingh's declaration) is the sole evidence supporting the patentee's statement that the Exela Defendants' allege constitutes a clear waiver of a pH of 6.8 and below.

Contrary to the Exela Defendants' argument, there is no clear disclaimer of a pH 6.8 and below in the prosecution history. While it is not entirely clear, the record suggests the 6.6 to 6.8 recitation was sloppiness on the part of the prosecuting attorney. This is true for at least two reasons: (1) the only described solutions of brimonidine previously administered to patients at 0.2% (w/v) – and thus the only solution capable of being compared with respect to efficacy with a 0.15% solution - were at pH 6.3 to 6.5, not 6.6 to 6.8; and (2) the only evidence submitted in support of the patentee's argument of a surprising finding relates to a 0.2% (w/v) brimonidine solution at pH 6.3 to 6.5. While it is difficult to know why the patentee used the 6.6 to 6.8 language in this sole, isolated incident, the use in this regard falls far short of a clear disclaimer of a pH 6.8 and below. Therefore, Apotex's construction should be adopted by this Court.

Apotex's construction mirrors the language of the claim itself and is more consistent with both the intrinsic evidence and this Court's own prior holdings.

CONCLUSION

Apotex respectfully requests the Court construe the claims according to the agreed-upon constructions of Apotex and Allergan as reflected in the parties' Revised Joint Claim Chart. (D.I. 46.)

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